ATTACHMENT A
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-45 (Canceled)

46. (New) A method for producing infectious hepacivirus-like particles ex vivo comprising the steps of:

- providing a first nucleic acid sequence comprising a packaging competent retroviral-derived genome;
- providing a second nucleic acid sequence comprising a cDNA encoding core proteins from said retrovirus;
- providing a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein;
- transfecting host cells with said nucleic acid sequences and maintaining the transfected cells in culture for sufficient time to allow expression of the cDNAs to produce structural proteins from hepacivirus and retrovirus; and allowing the structural proteins to form virus-like particles.

47. (New) The method according to claim 46, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

48. (New) The method according to claim 46, wherein said packaging competent retroviral-derived genome and core proteins are from a retrovirus selected from the group consisting of MLV, ALV, RSV, MPMV, HIV-1, HIV-2, SIV, EIAV, CAEV, or HFV.

49. (New) The method according to claim 47, wherein said polyprotein comprises a hepacivirus core protein and a hepacivirus E1 protein.

50. (New) The method according to claim 47, wherein said polyprotein comprises a hepacivirus core protein and a hepacivirus E2 protein.

51. (New) The method according to claim 46, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a hepacivirus p7 protein.

52. (New) The method according to claim 46, wherein said polyprotein comprises native hepacivirus E1 and/or E2 protein, and optionally native hepacivirus p7 protein.

53. (New) The method according to claim 47, wherein said polyprotein comprises a native hepacivirus core protein, a native hepacivirus E1 protein and native hepacivirus E2 protein, and optionally a native p7 protein.

54. (New) The method according to claim 47, wherein core protein, E1 protein and E2 protein, and optionally p7 protein, are derived from a same hepacivirus.

55. (New) The method according to claim 54, wherein said hepacivirus is a hepatitis C virus (HCV).

56. (New) The method according to claim 55, wherein said HCV core protein comprises the last 21 amino acids of the carboxy-terminus of HCV core.

57. (New) The method according to claim 54, wherein said E2 protein is a mutated E2 protein selected from the group consisting of a E2 protein deleted from its C-terminal

amino acid residue, and a native E2 protein wherein the hypervariable region 1 (HRV1) has been deleted.

58. (New) The method according to claim 46, wherein said nucleic acid sequence comprising a packaging competent retroviral-derived genome further comprises a transgene.

59. (New) An infectious hepacivirus-like particle obtainable by a method claim 46, comprising the core proteins from a retrovirus, and a E1 hepacivirus glycoprotein and/or a E2 hepacivirus glycoprotein.

60. (New) The infectious particle according to claim 59, comprising E1 and E2 hepacivirus glycoproteins.

61. (New) The infectious particle according to claim 59, comprising E1 hepacivirus glycoprotein.

62. (New) The infectious particle according to claim 59, comprising E2 hepacivirus glycoprotein.

63. The infectious particle according to claim 59, further comprising a hepacivirus p7 protein.

64. (New) The infectious particle according to claim 59, comprising native E1 and/or E2 hepacivirus glycoprotein, and optionally native p7 protein.

65. (New) The infectious particle according to claim 65, wherein core E1 and E2 protein, and optionally p7 proteins, are derived from a same hepacivirus.

66. (New) The infectious particle according to claim 65, wherein said hepacivirus is HCV.

67. (New) The infectious particle according to claim 66, wherein said E2 protein is a mutated E2 protein selected from the group consisting of a native E2 protein deleted from its C-terminal amino acid residue, and a native E2 protein wherein the hypervariable region 1 (HRV1) has been deleted.

68. (New) The infectious particle according to claim 59, wherein said retrovirus is selected from the group consisting of MLV, ALV, RSV, MPMV, HIV-1, HIV-2, SIV, EIAV, CAEV, or HFV.

69. (New) The infectious particle according to claim 59, wherein said nucleic acid sequence comprising a packaging competent retroviral-derived genome further comprises a transgene.

70. (New) A method for producing hepacivirus-like particles ex vivo comprising the steps of:

- providing a first nucleic acid sequence comprising a packaging competent retrovirus-derived genome;
- providing a second nucleic acid sequence comprising a cDNA encoding the core proteins from said retrovirus;
- providing a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, preferably a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein;
- transfecting host cells with said nucleic acid sequences and maintaining the transfected cells in culture for sufficient time to allow expression of the cDNAs to produce structural proteins from hepacivirus and retrovirus; and allowing the structural proteins to form virus-like particles.

71. (New) A method for producing hepacivirus-like particles in vivo, which method comprises the steps of :

- providing a first nucleic acid sequence comprising a packaging competent retrovirus-derived genome;

- providing a second nucleic acid sequence comprising a cDNA encoding the core proteins from said retrovirus;

- providing a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, preferably a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein;

- transfecting cells of a subject in vivo with said nucleic acid sequences, to allow expression of the cDNAs to produce structural proteins from hepacivirus and retrovirus; and to allow the structural proteins to form virus-like particles.

72. (New) The method according to claim 70 wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

73. (New) The method according to claim 72, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a hepacivirus p7 protein.

74. (New) The method according to claim 70, wherein said hepacivirus is HCV.

75. (New) A method for ex vivo identification of a receptor for hepacivirus E1 and/or E2 glycoprotein comprising detection of the binding of an infectious particle according to claim 59, to a cell receptor.

76. (New) A method for ex vivo identifying a cell receptor for hepacivirus comprising the step consisting of:

- transfecting a cell which is not permissive for hepacivirus infection with a nucleic acid sequence encoding a protein likely to be a receptor for hepacivirus;

- contacting said transformed cell with a hepacivirus-like particle according to claim 59;

- determining whether said transformed cell has become permissive or not for hepacivirus infection; and

- identifying as a cell receptor for hepacivirus said protein expressed by the transformed cell that has become permissive.

77. (New) A method for ex vivo identifying a cell receptor for a hepacivirus comprising the step consisting of:

- providing an expression cDNA library obtained from a cell permissive for hepacivirus infection;

- transfecting cells that are not permissive for hepacivirus infection with said expression cDNA library;

- contacting said transformed cells with hepacivirus -like particles according to claim 59;

- identifying and isolating those transformed cells that have become permissive for hepacivirus infection;

- isolating the expression vector transfected in cells that have become permissive; and

- identifying as a receptor for hepacivirus the proteins encoded by the cDNA sequence of said isolated expression vectors.

78. (New) A method of ex vivo screening or identification of molecules capable of interfering with hepacivirus entry in cells comprising comparison of the level of cell infection by an infectious particle according to claim 59 in the presence or the absence of a candidate molecule.

79. (New) A method of in vitro diagnosis of a hepacivirus infection in a patient, comprising detecting immune complexes formed by interaction of anti-hepacivirus antibodies likely to be present in a biological sample of the patient with hepacivirus-like particle according to claim 59.

80. (New) A method of in vitro diagnosis of a hepacivirus infection in a patient, comprising detecting an inhibitory effect of anti-hepacivirus antibodies likely to be present in a biological sample of the patient, on the infection of a permissive cell by hepacivirus-like particles according to claim 59.

81. (New) A diagnostic kit useful useful for the method of in vigtro diagnosis of a hepacivirus infection in a patent comprising a hepacivirus-like particle according to claim 59 and appropriate means of detection of said immune complexes.

82. (New) A vaccine composition comprising a hepacivirus-like particle according to claim 59 and a pharmaceutically acceptable carrier.

83. (New) A method for in vivo or in vitro transferring a transgene of interest in a cell, which method comprises infecting a cell with a hepacivirus-like particle according to claim 59, wherein the particle carries a transgene of interest.

84. (New) A transformed host cell that contains :

- a first nucleic acid sequence comprising a packaging competent retrovirus-derived genome;

- a second nucleic acid sequence comprising a cDNA encoding the core proteins from said retrovirus; and

- a third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a signal peptide from a type I membrane protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

85. (New) The transformed host cell according to claim 84 wherein said third nucleic acid sequence comprising a cDNA encoding a polyprotein comprising successively a hepacivirus core protein, and a hepacivirus E1 protein and/or a hepacivirus E2 protein.

86. (New) The transformed host cell according to claim 84, wherein said third nucleic acid sequence comprises a cDNA encoding a polyprotein that further comprises a HCV p7 protein.

87. (New) The transformed host cell according to claim 84, wherein said hepacivirus is HCV.

88. (New) A method of ex vivo screening of molecules capable of interfering with hepacivirus entry in cells comprising comparing the level of fusion of a transformed host cell according to claim 84 to a target host cell, in the presence or the absence of a candidate molecule.

89. (New) The method according to claim 88, comprising the steps consisting of:

- co-culturing said transformed host cell with a target host cell, in the absence or presence of a candidate molecule, under conditions that allow syncytia formation, i.e. cell-cell fusion, and hepacivirus-like particle entry in target host cell in the absence of any candidate molecule;
- assessing syncytia formation in the absence or in the presence of said candidate molecule;

- comparing syncytia formation measured in presence of said candidate molecule with syncytia formation measured in absence of any candidate molecule;

- identifying as a molecule capable of interfering with hepacivirus entry the candidate molecule for which syncytia formation, as measured in the presence of said molecule, is decreased as compared to syncytia formation measured in the absence of any candidate molecule.

90. (New) The method, according to claim 75, wherein said hepacivirus is HCV.